

What is claimed is:

1. A method of countering the development of resistance in a parent target to a parent neutralizing agent or countering the development of neutralizing activity in a parent neutralizing agent to a parent target comprising coevolving said parent target and said parent neutralizing agent, wherein said coevolving comprises diversifying each of said parent target and said parent neutralizing agent in vitro.
2. The method of claim 1 wherein said diversifying comprises generating a population of targets and neutralizing agents by mutagenesis, recombinant methods, or combinatorial synthetic methods.
3. The method of claim 1 wherein said coevolving comprises diversifying said parent target and said parent neutralizing agent, selecting one or more next generation neutralizing agents and next generation targets from diversified populations resulting from said diversifying, wherein the selected one or more neutralizing agents and targets have improved neutralizing activity and resistance, respectively, and optionally repeating said diversifying and selecting using said one or more next generation neutralizing agents or next generation targets.
4. The method of claim 3 wherein said improved neutralizing activity is neutralizing activity against said parent target or a previously selected next generation target.
5. The method of claim 3 wherein said improved resistance is resistance to a said parent neutralizing agent or a previously selected next generation neutralizing agent.
6. The method of claim 3 wherein said repeating is continued until a neutralizing agent having a desired neutralization profile is identified, until a target having a desired resistance profile is identified, or until no further neutralizing agent or targets having improved neutralizing activity or resistance are identified.
7. The method of claim 6 wherein said desired neutralization profile is broad neutralizing activity.

8. The method of claim 6 wherein said desired resistance profile is broad resistance.
9. The method of claim 1 wherein said parent neutralizing agent is a cell, protein, nucleic acid, small molecule, bacterium, or virus.
10. The method of claim 1 wherein said parent neutralizing agent is an antibody.
11. The method of claim 1 wherein said parent target is a cell, protein, nucleic acid, small molecule, bacterium, or virus.
12. The method of claim 1 wherein said parent target is an antigen.
13. A method of preparing a neutralizing agent having a desired neutralization profile or a target having a desired resistance profile comprising:
 - a) coevolving a parent target and a parent neutralizing agent pair to generate a collection of evolved neutralizing agents and a collection of evolved targets;
 - b) cross testing members of said collections for neutralizing activity or resistance; and
 - c) identifying at least one member of said collection of evolved neutralizing agents having said desired neutralizing profile or identifying at least one member of said collection of evolved targets having said desired resistance profile.
14. The method of claim 13 further comprising optionally repeating said coevolving using the identified members of step c).
15. The method of claim 13 wherein said desired neutralizing profile is broad neutralizing activity.
16. The method of claim 13 wherein said at least one neutralizing agent identified in step c) has neutralizing activity against the greatest number of tested members of said collection of evolved targets.
17. The method of claim 13 wherein said desired resistance profile is broad resistance.

18. The method of claim 17 wherein said broad resistance is resistance to the greatest number of tested members of said collection of evolved neutralizing agents.
19. The method of claim 13 wherein said parent neutralizing agent or parent target is a cell, protein, nucleic acid, small molecule, bacterium, or virus.
20. The method of claim 13 wherein said parent neutralizing agent is an antibody.
21. The method of claim 13 wherein said parent target is an antigen, cell, bacterium, or virus.
22. The method of claim 13 wherein said parent target is an antigen.
23. The method of claim 13 further comprising repeating steps a) to c) using the identified neutralizing agents or targets of step c) in said coevolving.
24. The method of claim 13 wherein said coevolving comprises diversifying said parent target and said parent neutralizing agent in vitro, selecting one or more next generation neutralizing agents and targets from populations resulting from said diversifying, wherein the selected one or more neutralizing agents and targets have new or improved neutralizing activity or resistance, respectively, and optionally repeating said diversifying and selecting using said one or more selected next generation neutralizing agents and next generation targets, wherein said parent neutralizing agent and the selected one or more neutralizing agents form a collection of evolved neutralizing agents and said parent target and the one or more selected targets form a collection of evolved targets.
25. The method of claim 13 wherein said coevolving comprises:
- i) contacting said parent neutralizing agent with members of an initial population of targets generated by diversifying said parent target in vitro;
 - ii) selecting one or more resistant targets within said initial population, wherein said one or more resistant targets has new or improved resistance to said parent neutralizing agent;

iii) diversifying said parent neutralizing agent to create a population of neutralizing agents;

iv) contacting members of said population of neutralizing agents with said one or more resistant targets selected in step ii);

v) selecting one or more further neutralizing agents from said population of neutralizing agents, wherein said one or more further neutralizing agents has new or improved neutralizing activity against said one or more resistant targets;

vi) optionally repeating steps i) and ii) or optionally repeating steps i), ii), iii), iv), and v) using said one or more further neutralizing agents in place of said neutralizing agent and using said one or more resistant targets in place of said target,

wherein said parent neutralizing agent and said one or more further neutralizing agents are members of a collection of evolved neutralizing agents, and wherein said parent target and said one or more resistant targets are members of a collection of evolved targets.

26. A method of coevolving, comprising:

a) diversifying in vitro a parent target and selecting at least one next generation target from a diversified population of targets resulting from said diversifying, wherein the selected at least one target has new or improved resistance to a parent neutralizing agent having neutralizing activity against said parent target; and

b) diversifying in vitro said parent neutralizing agent and selecting at least one next generation neutralizing agent from a diversified population of neutralizing agents resulting from said diversifying, wherein the selected at least one neutralizing agent has new or improved neutralizing activity against said selected at least one target.

27. The method of claim 26 further comprising repeating step a) or repeating steps a) and b) one or more times, wherein each diversifying step produces a diversified population of the at least one target or neutralizing agent that was previously selected.

28. A method of coevolving, comprising:

a) diversifying a parent neutralizing agent and selecting at least one next generation neutralizing agent from a diversified population of neutralizing agents resulting from said diversifying, wherein the selected at least one neutralizing agent has new or improved

neutralizing activity against a parent target having resistance to said parent neutralizing agent; and

b) diversifying said parent target and selecting at least one next generation target from a diversified population of targets resulting from said diversifying, wherein the selected at least one target has new or improved resistance to said selected at least one neutralizing agent.

29. The method of claim 28 further comprising repeating step a) or repeating steps a) and b) one or more times, wherein each diversifying step produces a diversified population of the at least one target or neutralizing agent that was previously selected.

30. A method of coevolving a parent target and parent neutralizing agent to produce a collection of evolved targets and a collection of evolved neutralizing agents, comprising:

i) contacting said parent neutralizing agent with members of an initial population of targets generated from said parent target;

ii) selecting one or more resistant targets within said initial population, wherein said one or more resistant targets has new or improved resistance to said parent neutralizing agent;

iii) diversifying said parent neutralizing agent to create a population of neutralizing agents;

iv) contacting members of said population of neutralizing agents with said one or more resistant targets selected in step ii);

v) selecting one or more further neutralizing agents from said population of neutralizing agents, wherein said one or more further neutralizing agents have new or improved neutralizing activity against said one or more resistant targets;

vi) optionally repeating steps i) and ii) or optionally repeating steps i), ii), iii), iv), and v) using said one or more further neutralizing agents in place of said parent neutralizing agent and using said one or more resistant targets in place of said parent target,

wherein said parent neutralizing agent and said further neutralizing agents are members of a collection of evolved neutralizing agents, and wherein said parent target and said resistant targets are members of a collection of evolved targets.

31. A method of treating or preventing a disease associated with a parent target, comprising administering to a patient having or predisposed to said disease a therapeutically effective amount of a neutralizing agent prepared by the method of claim 30, wherein said neutralizing agent is a small molecule.
32. The method of claim 31 wherein said disease is a bacterial or viral infection.
33. The method of claim 31 wherein said disease is cancer.
34. A method of developing a desired characteristic in a parent antibody or parent target comprising coevolving said parent antibody and parent target, wherein said coevolving comprises diversifying each of said parent antibody or parent target in vitro.
35. The method of claim 34 wherein said diversifying is carried out by mutagenesis or recombinant methods.
36. A method of preparing an antibody having broadened neutralizing activity compared with a parent antibody comprising coevolving said parent antibody and a parent target.
37. The method of claim 36 wherein said parent target is a pathogen or protein.
38. An antibody prepared by the method of claim 36.
39. A composition comprising an antibody and a pharmaceutically acceptable carrier, wherein said antibody is prepared by the method of claim 36.
40. A method of treating or preventing a disease associated with a parent target, comprising administering to a patient having or predisposed to said disease a therapeutically effective amount of antibody prepared by the method of claim 36.
41. The method of claim 40 wherein said disease is a bacterial or viral infection.
42. The method of claim 40 wherein said disease is cancer.

43. A method of preparing an antigen having broadened antigenic activity compared with a parent antigen comprising coevolving said parent antigen and a parent neutralizing agent.
44. An antigen prepared by the method of claim 43.
45. A composition comprising an antigen and a pharmaceutically acceptable carrier, wherein said antigen is prepared by the method of claim 43.
46. A method of preventing a disease or condition associated with a parent antigen, comprising administering to a patient having or predisposed to said disease or condition an amount of preventative antigen sufficient to prevent said disease or condition, wherein said preventative antigen is prepared by the method of claim 43.
47. The method of claim 46 wherein said preventative antigen has broadened antigenic activity compared with said parent antigen.
48. The method of claim 46 wherein said disease or condition is a bacterial or viral infection.
49. The method of claim 46 wherein said disease or condition is cancer.
50. The method of claim 46 wherein said disease or condition is an allergy.